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Malignant melanoma revealed by testicular metastasi.

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ABSTRACT

We report the case of an 83 years old man supported for painless indurated and nodular lesion of the left testicle. Histological analysis identified a primary cutaneous melanoma metastasis although it has never been found on physical examination.

The discovery of a testicular mass should suggest first a germ cell tumor, despite in some populations (age over 60 years), other diagnosis are more frequent, including metastasis.

Due to rapid disease progression and high mortality rate within a short interval, a complete staging looking for other secondary locations must be done and a multidisciplinary care and palliative involvement must also be initiated in the context of metastatic melanoma.

1. Introduction

Cutaneous malignant melanoma diagnosed by a testicular metastasis is uncommon.

Although germ cell tumors are the most frequent tumors in men after age 65 other diagnostics should be mentioned as lymphoma and melanoma. We report the case of an 83 years old man with a testicular mass revealing a metastatic melanoma.

2. Case report

An 83 years old man was seen for a mild but rapidly evolving deterioration of his general state, associated with a testicular tumefaction. He had a body mass index of 19.3 kg/m^2 and a loss of 14 kg from is usual weight. His WHO performance status was 2–4. Physical examination before surgery did not show any skin lesion but only bilateral superficial inguinal lymphadenopathies.

The scrotal ultrasound revealed a hypoechoic, heterogeneous, well-limited nodule, measuring 14 per 20 mm, with a central and peripheral hypervascularization on the Doppler, associated with multiple bilateral nodules in the subcutaneous tissue of the scrotum.

A total left orchidectomy with testicular prosthesis replacement using an inguinal approach was performed, for a diagnostic purpose.

The surgical approach was responsible for the incidental finding of a subcutaneous necrotic left inguinal nodule, highly friable, measuring 2 cm.

Macroscopic analysis of the resected specimen showed an indurated, brown nodule of 2.2 cm long in its greater axis, strongly evocative of a testicular melanoma (Fig. 1).

Microscopic analysis showed cells arranged in clusters, without specific tissue architecture, with a dark brown intracytoplasmic pigment, a megakarycytosis, a high mitotic index, and an important infiltration of the underlying fatty tissue (Fig. 2).

The immuno-histological profile confirmed a testicular melanoma metastasis (Fig. 3). The search of BRAF mutation was negative.

After surgery, the patient had many subcutaneous nodules appearing on the whole body and cervical, axillary and inguinal lymphadenopathies.

A thoracic abdominal and pelvic CT-scan, realized postoperatively, revealed nodules suggestive of metastasis in lungs, soft tissues, hepatic fundus, adrenal glands, anterior mediastinum, thyroid gland, pericardium, and an osteolytic lesion of the third lumbar vertebra (Fig. 4). These locations are not usual secondary locations for germ cells tumors.

In this context of multi metastatic melanoma, a cerebral MRI was performed. It revealed diffuse supra and infratentorial lesion of the brain, including one in the third ventricle, without impact on the ventricular system (Fig. 5).

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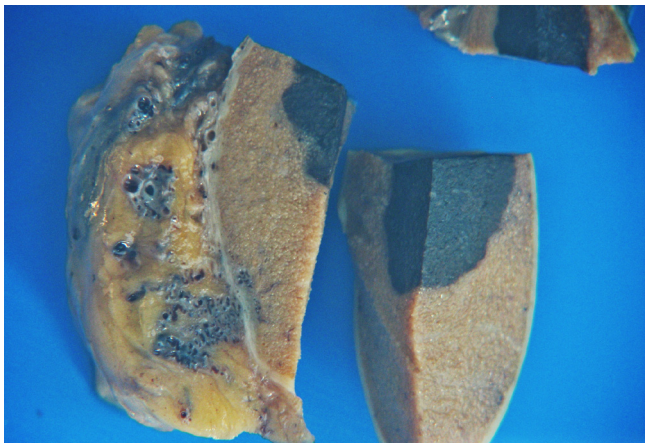

Fig. 1. Macroscopic view of the testicular specimen. Melanoma appears in dark blue.

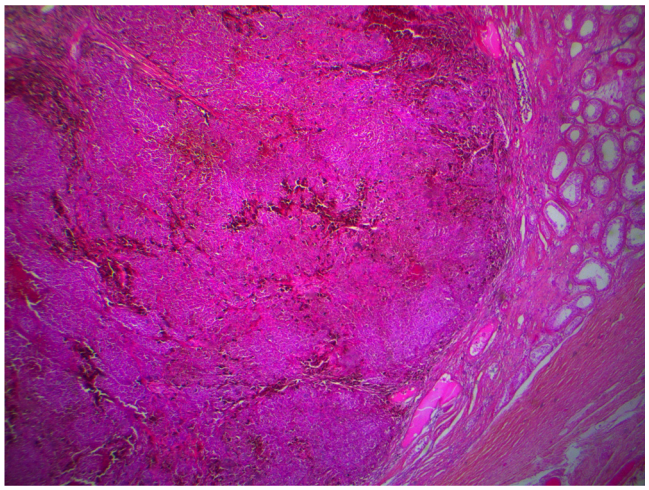

Fig. 2. Microscopic view, nodular tumor, poorly circumscribed, composed of nests of cells with frequent clusters of brown pigment (dark arrow). Testicular parenchyma is visible on the periphery (blue arrow). Magnification x25, HES stain.

A per os chemotherapy containing temozolomide was administrated, only 3 doses in 5 days because of the poor tolerance with increased confusion.

Because of the confusion, a lumbar puncture was performed and demonstrated meningeal carcinomatosis.

The patient received a palliative care because of the increase of confusion and major deterioration of the general state.

The patient died of a status epilepticus caused by cerebral metastasis a little less than 2 months after the orchidectomy.

3. Discussion

Melanoma affects people of all ages. Its occurrence is very rare before puberty. Its incidence doubles every 10 years (especially in countries where the sun exposure is important and where the population is mainly Caucasian). Its death rate is 1.7 for 100,000 for men in France in 2011 [1].

Testicular tumors affect mainly young adults and are generally germ cells tumors. However, after age 60, epidemiological data are different, though their clinical presentations remain the same (occurring under the form of a nodule or a painful testicular mass) [2].

The diagnosis of skin melanoma is mainly clinical, with the use of a dermatoscope. It is usually an incidental diagnosis, rarely established on clinical signs (such as morphological modifications of a nevi, or alteration of the general state).

The most commonly used prognostic histological score is the Breslow index (thickness of the tumor, measured on the specimen, between the stratus granulosus and the deepest layer of the tumor), and Clark index (the degree of invasion of tumoral cells in the dermo-hypodermic layers, its value is less important than the Breslow index). The ulceration and mitotic index are also highly predictive elements [3].

Its extension work up depends on the causal lesion, the lymphatic drainage zone ultrasounds assessment is optional and every other paraclinical examination depends on clinical calling-in points. The histopathological examination and extension work up for the staging of the cancer follow the UICC/AJCC classification.

A life-long follow up will be ensured, its frequency depending on the seriousness of the initial lesion [4].

According to the French Urologic Lesions Study Group (GELU) concerning 2215 testicular tumors diagnosed in 13 French centers, the most commonly encountered malignant testicular tumors histological types after age 60 are, in order of frequency: blood disease (31.92%), germ cells tumors (18.78%), Leydig cells tumors (9.86%), metastasis (9.39%), benign mesenchymal tumors (7.98%), sarcomas (7.51%), adenomatoid tumors (3.29%), spermatocytic seminomas (1.88%), epidermal cysts (1.41%) and other types (7.98%).

Testicular metastasis is rarely symptomatic of an unrecognized cancer (less than 15%) [5,6].

A testicular mass after age 65 has to evoke a secondary lesion, even though lymphoma remains the most frequent diagnosis.

There are other symptoms evoking a testicular melanoma, such as: absence of elevation of tumor markers, presence of melanospermia, presence of a supraclavicular lymphadenopathy, and personal history of skin primitive melanoma [7].

Life expectancy of patients having a testicular metastis is very low, because of the advanced stage of tumoral spreading [8].

The main differential diagnoses in males after age 65 are: diffuse large B cells lymphoma (CD20+), germ cells tumors and Leydig cells tumors.

There are various ways of spreading for testicular metastasis: retrograde venous way, arterial embolism, lymphatic route, or by contiguity with the primary lesion.

It is also possible for the lesion to regress and to make way for a systemic dissemination, like in the present case, though this event is very rare.

The diagnostic approach is to identify before treating the primitive lesion. However, if the lesion remains unidentified, and since there is no more easily accessible metastatic lesion, the diagnostic process consists in radical orchiectomy through inguinal approach after high spermatic cord ligation, followed by histopathologic examination.

Some histological elements can lead to suspect a testicular metastasis [9]:

- morphological aspect that does not evoke a primitive testicular tumor
- predominant interstitial infiltration sparing the seminar ducts
- numerous lymphatic and vascular emboli in the testis, epididymis and spermatic cord.
- misleading signs: predominant intratubular extension mimicking intratubular germ cell neoplasia (27% of cases) invading the rete testis.

Histologic examination succeeds in a great majority of cases in identifying the primitive tumor and in eliminating differential diagnoses. Specific immunohistochemical markers of melanoma are: PS100, Melan A, HMB45.

According to the GELU study, cancers metastasizing in testicles are, in order of frequency: prostate adenocarcinomas (30–65%),

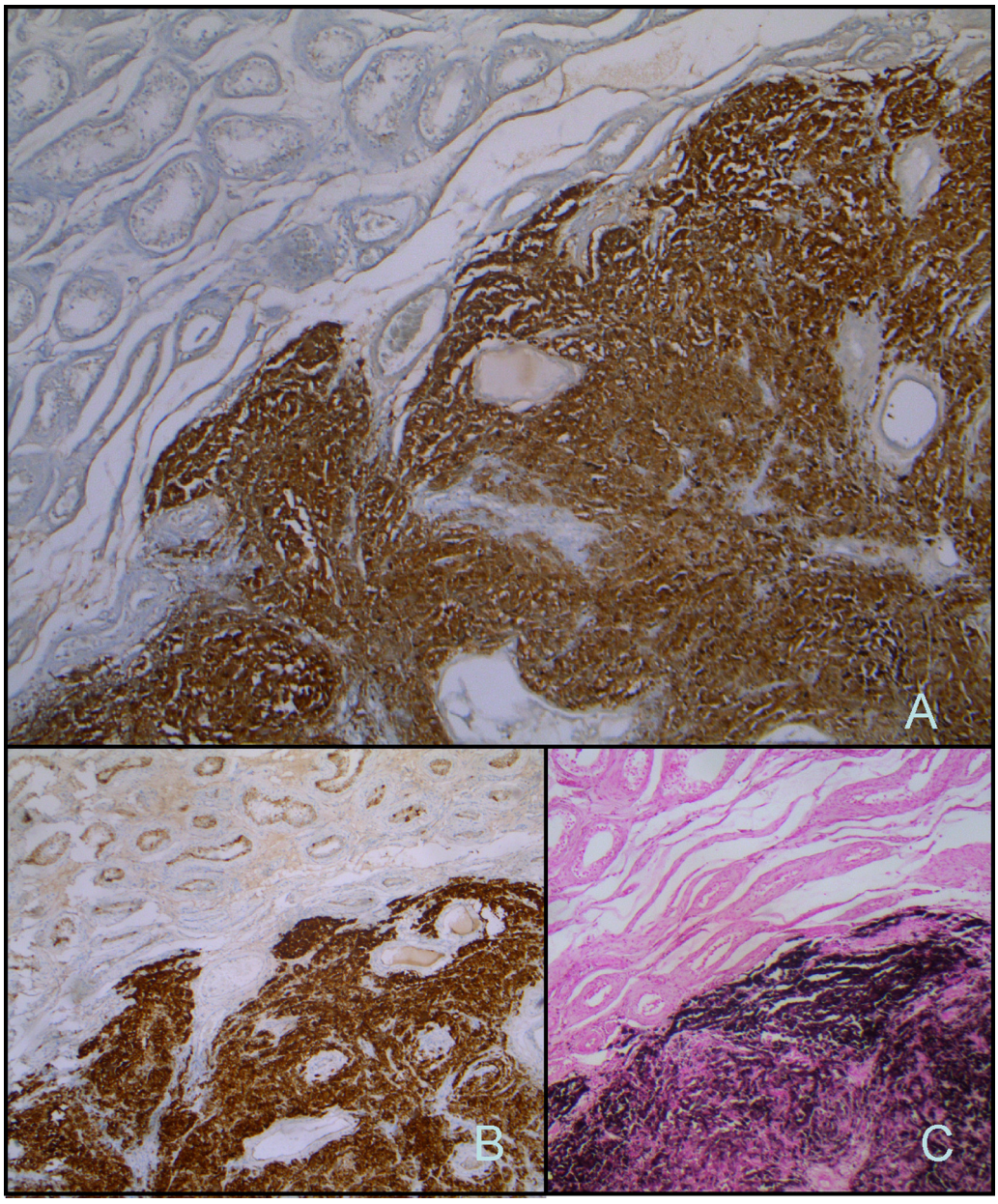

Fig. 3. Immuno-histological profile by PS100 (A), Melan A (B), two markers of melanocytic differentiation. Fontana's stain shows the melanic pigment in black (C).

bronchopulmonary carcinomas (20%), skin melanomas (10%), kidney, colon, and upper respiratory and gastro-intestinal carcinomas (<10%) [2,10].

Their treatment and evolution depend on the underlying disease. Testicular melanoma metastases with skin in transit metastases are not rare, it is however really uncommon for the primitive tumor not to be discovered. 15% of skin melanomas metastasize in the testicles, but they are almost exclusively diagnosed at the autopsy, because they are not much symptomatic, the primitive tumor is unknown, and these secondary lesions are sign of an advanced stage cancer. It explains why most of the epidemiological data come from post mortem examination series, in which from 9% to 41% of testicular metastases are originated from primitive skin melanomas [11].

The series of autopsy of the Memorial Hospital and MD Andersen indicates that 8% of patients with disseminated melanoma had testicular metastases but none of these metastases had been clinically diagnosed before the patient's death.

Fig. 4. Axial view of the abdominal CT scan with subcutaneous nodules suggestive of metastasis (white arrow).

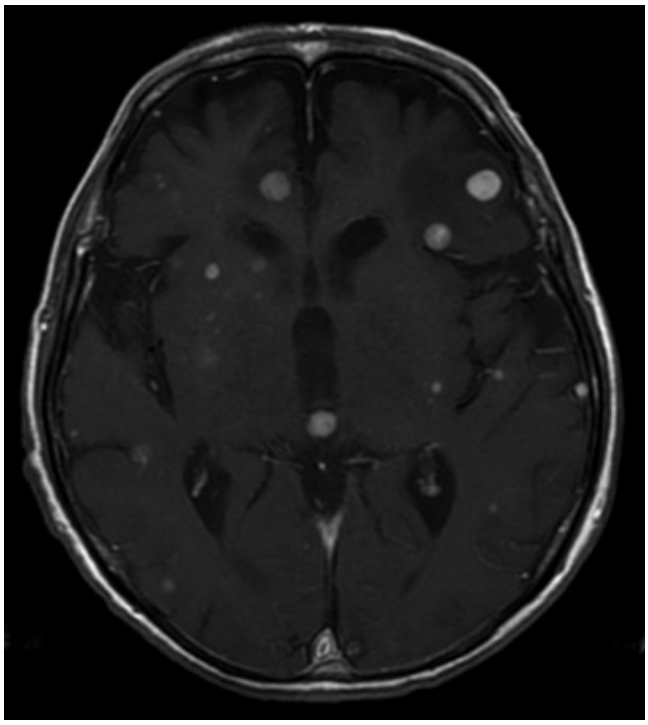

Fig. 5. Axial view of the brain MRI with gadolinium injection: enhancement of brain metastasis, which appears in white circular lesions.

In this publication the various histological types of testicular tumor were, by frequency: germinal tumors (85%), non-Hodgkin's lymphoma (main differential diagnosis for a testicular nodule after the age of 65), endocrine tumors, Sertoli cell tumors (5%) and rare forms: embryonal carcinoma, yolk sac tumor, choriocarcinoma, teratocarcinoma and melanoma [12].

The testicular metastases of melanoma are the most aggressive and they sign a progressive and severe illness. The prognosis is poor with extremely high and rapid mortality, with in most cases a survival lower than 12 months between the orchidectomy and the death [2].

Any scrotal mass after the age 65 should lead to investigation for a primitive cutaneous melanoma, but its absence does not eliminate the diagnosis. Testicular metastases of cutaneous malignant melanoma are of extreme severity due to the advanced stage of the disease. Early oncology care is needed to improve the survival of these patients of very poor prognosis.

Conflicts of interest

No conflict of interest.

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Ethical approval

No ethical approval needed.

Consent

The consent was impossible to obtain because the patient in this case report died 2 years ago and his relatives were not retrievable.

Author contribution

Dusaud Marie: writing and concept design.
Adjadj Lucille: writing and data collection.
Debelmas Alexandre: writing.
Souraud Jean Baptiste: pathologist, data collection.
Durand Xavier: managing the writing, concept design.

Guarantor

Dusaud Marie.

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